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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.
08/663,272	11/25/96	HARRISON	L 10308

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EXAMINER	
EWOLDT,G	
ART UNIT	**PAPER NUMBER**
1644	28

DATE MAILED: 10/25/01

Please find below and/or attached an Office communication concerning this application or proceeding.

Commissioner of Patents and Trademarks

Office Action Summary

Application No.	Applicant(s)
08/663,272	Harrison et al.
Examiner	**Art Unit**
G. R. Ewoldt	1644

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136 (a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1) ☒ Responsive to communication(s) filed on *Aug 22, 2001* .

2a) ☐ This action is **FINAL.** 2b) ☒ This action is non-final.

3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11; 453 O.G. 213.

Disposition of Claims

4) ☒ Claim(s) *39, 40, 42, and 43* is/are pending in the application.

4a) Of the above, claim(s) _____ is/are withdrawn from consideration.

5) ☐ Claim(s) _____ is/are allowed.

6) ☐ Claim(s) _____ is/are rejected.

7) ☒ Claim(s) *39, 40, 42, and 43* is/are objected to.

8) ☐ Claims _____ are subject to restriction and/or election requirement.

Application Papers

9) ☐ The specification is objected to by the Examiner.

10) ☐ The drawing(s) filed on _____ is/are objected to by the Examiner.

11) ☐ The proposed drawing correction filed on _____ is: a) ☐ approved b) ☐ disapproved.

12) ☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. § 119

13) ☒ Acknowledgement is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d).

a) ☒ All b) ☐ Some* c) ☐ None of:

1. ☒ Certified copies of the priority documents have been received.
2. ☐ Certified copies of the priority documents have been received in Application No. _____ .
3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

*See the attached detailed Office action for a list of the certified copies not received.

14) ☐ Acknowledgement is made of a claim for domestic priority under 35 U.S.C. § 119(e).

Attachment(s)

15) ☒ Notice of References Cited (PTO-892)
16) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
17) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s). _____
18) ☐ Interview Summary (PTO-413) Paper No(s). _____
19) ☐ Notice of Informal Patent Application (PTO-152)
20) ☐ Other:

DETAILED ACTION

1. The examiner of your application in the PTO has changed. To aid in correlating any papers for this application, all further correspondence regarding this application should be directed to Dr. Gerald Ewoldt, Art Unit 1644.

2. Claims 39-40 and 42-43 are pending.

3. In view of Applicant's amendment and response, filed 8/22/01, the previous rejections of Claims 39-40 and 43 have been withdrawn.

4. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

5. Claim 42 stands rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains or with which it is most nearly connected to make and/or use the invention, for the reasons of record as set forth in Paper No. 25, mailed 2/21/01.

Note that Applicant has amended Claim 39 to remove "derivatives", but said language is still pending in Claim 42.

6. The following is a new ground of rejection.

7. Claims 39-40 and 42-43 are rejected under 35 U.S.C. 112, first paragraph, because the specification does not reasonably provide enablement for a method of treating subjects with insulin dependent diabetes mellitus (IDDM) comprising administering to said subject the claimed peptides.

The specification discloses only that the peptides consisting of SEQ ID NOS:1 and SEQ ID NOS:2 can induce the *in vitro* proliferation of T cells obtained from some IDDM-at risk subjects as well as some control subjects. Said disclosure is insufficient to support the claimed methods. The specification fails to establish any connection between the claimed peptides' ability to cause T cells to proliferate *in vitro* and an ability

to provide an effective treatment for IDDM (see below for enablement of peptide therapy). Assuming *arguendo*, that some connection between the experimental data and the claimed methods could be established, it is unclear how the data of the instant examples could be used to support said claimed method. Given the huge ranges of the T cell proliferative responses (with standard errors approaching 50%) and the fact that the peptides caused proliferation in some control experiments while failing to cause proliferation in some of the experiments using IDDM-at risk T cells, it appears the instant data must be considered non-conclusive.

Note that the first line of the specification discloses that the peptides of the instant claims are intended to "interact immunologically with antibodies or T cells in subjects having pre-clinical or clinical Insulin-Dependent Diabetes Mellitus (IDDM)." So while the claimed peptides have not been claimed as pharmaceutical compositions, it is clear that such is their intended use, thus, requiring *in vivo* enablement for the intended pharmaceutical use. Pharmaceutical uses include the *in vivo* diagnosis, prevention, treatment, or cure of a disease or condition. The specification, however, provides no working examples demonstrating enablement for any *in vivo* uses of the claimed peptides as discussed above. While working examples can not be required, the induction of specific tolerance is highly complex and unpredictable, thus, requiring enablement in addition to mere assertion that the claimed invention word work. As taught by Tisch et al. (1994), it is apparent that peptide- or antigen-specific T immunotherapy, when applied to a highly defined animal model of autoimmunity, can be effective. However, it is unclear whether this approach is feasible in the prevention or treatment of spontaneous human autoimmune disease such as IDDM, in which the target autoantigens are not known, or in which a number of autoantigens appear to be involved in the disease process. Furthermore, it is unclear whether such immunotherapy can be used to treat an ongoing autoimmune response (i.e., after the onset of symptoms, such as in IDDM) or whether it is effective only in terms of prevention. The reference further teaches that in some instances, peptide therapy actually exacerbates the disease condition. Thus, peptide treatment of any autoimmune condition must be considered highly unpredictable, requiring a specific demonstration of efficacy on a case by case basis. Absent said demonstration, the invention would require undue experimentation to practice as claimed.

In re Wands, 858 F.2d at 737, 8 USPQ2d at 1404 (Fed. Cir. 1988) indicates that the more unpredictable an area is, the more

specific enablement is necessary in order to satisfy the statute. Thus, in view of the quantity of experimentation necessary, the lack of working examples, the unpredictability of the art, and the lack of sufficient guidance in the specification, it would take undue trials and errors to practice the claimed invention.

8. The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

9. Claims 39 and 42 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. Specifically, it is unclear how a sequence can consist of 15 residues and fall within the 13 amino acid stretch of amino acids 506 to 518 of GAD65 or the 13 amino acid stretch of amino acids 24 to 36 of human proinsulin.

10. No claim is allowed.

11. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Dr. Gerald Ewoldt whose telephone number is (703) 308-9805. The examiner can normally be reached Monday through Thursday from 7:30 am to 5:30 pm. A message may be left on the examiner's voice mail service. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Christina Chan can be reached on (703) 308-3973. Any inquiry of a general nature or relating to the status of this application should be directed to the Technology Center 1600 receptionist whose telephone number is (703) 308-0196.

Papers related to this application may be submitted to Technology Center 1600 by facsimile transmission. Papers should be faxed to Technology Center 1600 via the PTO Fax Center at (703) 305-3014.

G.R. Ewoldt, Ph.D.
Patent Examiner
Technology Center 1600
October 24, 2001

Patrick J. Nolan, Ph.D.
Primary Examiner
Technology Center 1600